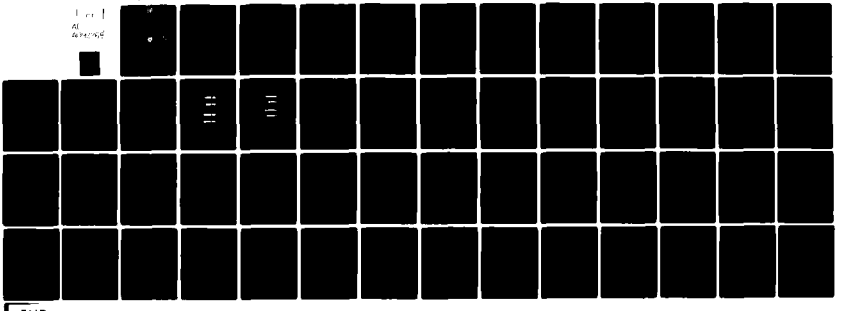
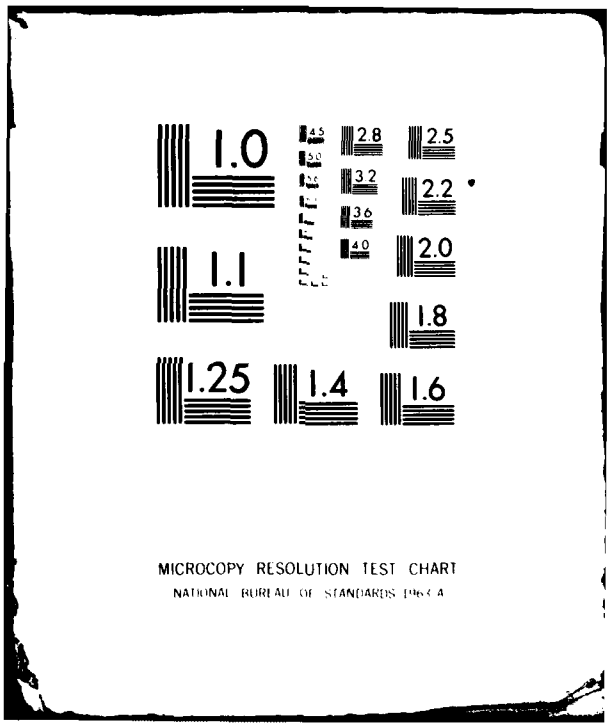
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EFFECTS OF OZONE (0.30 PARTS PER MILLION, 600 $\mu g/m^3$) ON SEDENTARY MEN REPRESENTATIVE OF AIRLINE PASSENGERS AND COCKPIT CREWMEMBERS

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(12) 54

DTIC ELECTE DEC 1 1980 C

March 1980

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U.S. DEPARTMENT OF TRANSPORTATION
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Technical Report Documentation Page

1. Report No.	2. Government Accession No.	3. Recipient's Catalog No.
FAA-AM-80-9	AD-A092268	

4. Title and Subtitle	5. Report Date
EFFECTS OF OZONE (0.30 PARTS PER MILLION, ~600 $\mu g/m^3$) ON SEDENTARY MEN REPRESENTATIVE OF AIRLINE PASSENGERS AND COCKPIT CREWMEMBERS	March 1980
	6. Performing Organization Code
7. Author(s) E. A. Higgins, M. T. Lategola, C. E. Melton, and J. A. Vaughan	8. Performing Organization Report No.
9. Performing Organization Name and Address FAA Civil Aeromedical Institute P.O. Box 25082 Oklahoma City, Oklahoma 73125	10. Work Unit No. (TRAIS) 11. Contract or Grant No. 13. Type of Report and Period Covered
12. Sponsoring Agency Name and Address Office of Aviation Medicine Federal Aviation Administration 800 Independence Avenue, S.W. Washington, D.C. 20591	14. Sponsoring Agency Code

15. Supplementary Notes

Work was done under approved Tasks AM-E-79-PHY-119 and AM-E-80-PHY-124.

16. Abstract

This study was undertaken to determine the effects of 0.30 ppmv ozone on 40 men representative of airline pilots. All were medically fit; 20 were smokers and 20 were nonsmokers. Subjects were divided into two age groups, 40-49 years and 50-59 years. The experiments consisted of exposure to 0.30 ppmv ozone and, on another occasion, to air only for 3 h at a simulated altitude of 6,000 ft mean sea level. Subjects were sedentary throughout the experiment. Ozone had no effect on heart rate and short-term memory. The group showed a statistically significant incidence of symptoms related to ozone exposure; most were shown by the 40- to 49-year-old nonsmoking group while at altitude and postaltitude, and in smokers in the 50- to 59-year age group only at altitude. Eye irritation was the commonest symptom, followed by headache, nasal irritation, and throat irritation. Data showed significant effects of ozone on forced expiratory volume, 1-second forced expiratory volume, and forced end-expiratory flow. The pulmonary effect of ozone appears to be principally on the small airways.

Impairment of visual accommodation was associated with ozone. Dark adaptation threshold was elevated in ozone in the 50- to 59-year nonsmoking age group. Retinal bleach recovery time was retarded and blink rate was higher during ozone exposure.

It is concluded that 0.30 ppmv ozone is near threshold for adverse effects of ozone. The data are also applicable to passengers who fit into the same category as these sedentary subjects.

17. Key Words	18. Distribution Statement
Air pollution, Ozone, Respiration, Vision, Heart rate, Short-term memory, Hand steadiness, Airline operations, Airline pilots, Airline passengers	Document is available to the public through the National Technical Information Service, Springfield, Virginia 22161.

19. Security Classif. (of this report)	20. Security Classif. (of this page)	21. No. of Pages	22. Price
Unclassified	Unclassified	45	

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PREFACE

The authors of this report are listed in alphabetical order because the contributions of each were substantially equal; thus, the order does not imply seniority.

The report is organized into sections as indicated in the Table of Contents to facilitate location of data of particular interest. Page numeration runs consecutively throughout the report; references are given at the end of each section.

The authors would like to acknowledge the contributions of several people without whom this work could not have been done. They are, in alphabetical order: Mary Jo Burr, Donna Fitzgerald, Patsy Fowler, Gordon Funkhouser, Peggy Lyne, Stanley Mullen, Clay Tucker, and Marlene Wicks. Special thanks are expressed to Drs. Samuel F. Flynn and Clyde Lynn who carried out the medical examinations on the subjects.

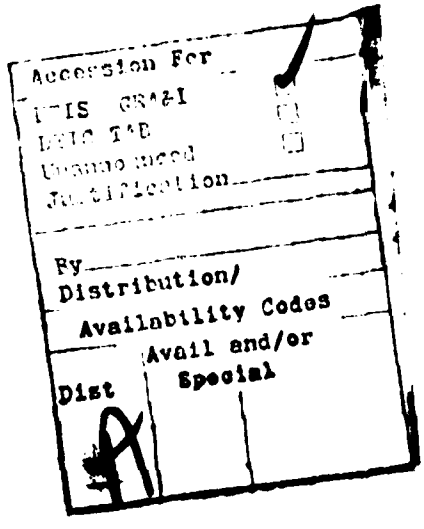


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SECTION I

INTRODUCTION

C. E. Melton

Research reported earlier (1) established that 0.30 parts per million by volume ozone (ppmv, $\sim$600 $\mu g/m^3$) was the threshold level for mild reversible pulmonary and visual effects on exercising men and women representative of the flight attendant population. The pulmonary effect consisted of a restriction of flow and volume of expired air. The effect was interpreted as being due to a constriction, obstruction, or collapse of terminal bronchioles, together with upper respiratory irritation leading to mild discomfort. The visual effects consisted of conjunctival and corneal irritation and reduced photopic visual acuity. The latter effect may have been secondary to eye irritation by causing tearing and/or corneal swelling. No effects by ozone were found on scotopic vision. This lack of effect was significant because an earlier report from another laboratory had reported positive findings in this regard (2).

No effects of ozone were found on blood cells or plasma; negative results were also found for urinary 17-ketogenic steroids and catecholamines.

Subjective effects of 0.30 ppmv ozone varied from one person to another and consisted of cough, nose and throat burning, eye irritation, substernal pain and headache. These symptoms outlasted the period of exposure to ozone by several hours to several days; all symptoms eventually disappeared, however. The effects attributed to ozone conformed generally to the symptoms reported by flight attendants.

Exercise was clearly an aggravating factor because 0.30 ppmv ozone was without marked effect on sedentary subjects representative of the flight attendant population. Exercise exacerbated the effects of ozone by increasing the rate and depth of respiration. Also, exercising subjects breathed through a mouthpiece, thus circumventing the ozone-scrubbing effect of nasal breathing. These findings led to the observation that nasal breathing and avoidance of exercise by passengers and crew would minimize effects of ozone exposure.

Female subjects showed quantitatively the same pulmonary effects shown by males but at a lower level of exercise, suggesting that females are more susceptible to ozone than are males. Fewer complaints of "ozone sickness" from flight deck crews than from flight attendants may be related to the fact that most pilots are males with sedentary duties, whereas most flight attendants are females and are physically active in flight.

The present study was undertaken to define the effects of 0.30 ppmv ozone on flight crew surrogates. The ozone concentration was chosen because, as outlined above, 0.30 ppmv was found to be the threshold level for effects on flight attendant surrogates.

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1. Higgins, E. A., M. T. Lategola, J. M. McKenzie, C. E. Melton, and J. A. Vaughan: Effects of Ozone on Exercising and Sedentary Adult Men and Women Representative of the Flight Attendant Population. FAA Office of Aviation Medicine Report No. FAA-AM-79-20, July 1979.

2. Lagerwerff, J. M.: Prolonged Ozone Inhalation and Its Effects on Visual Parameters, AEROSP. MED., 34:479-486, 1963.

SECTION II

GENERAL METHODS

C. E. Melton

Age, height, and weight characteristics of the subject population are shown in Table 1. All subjects were given a medical examination prior to their acceptance as subjects. Those who were found medically fit were fully briefed on the purposes, procedures, and hazards of the project. Each subject then signed an informed consent document and was given training at altitude on each experimental test.

The actual experimental sessions consisted of exposure on one occasion to 0.30 ppmv ozone and, on another occasion, to air only for 3 h in a hypobaric chamber at a simulated altitude of 6,000 ft above mean sea level (MSL). The order of presentation of experimental conditions was balanced; i.e., half the subjects were exposed to ozone first and half to air only first. Exposures were separated by 1 week. Each subject thus served as his own control.

When subjects reported to the laboratory at 0800 for experimental sessions, they changed into a surgical scrub suit and were given initial tests as detailed in later sections of this report. Each subject was then given a standard breakfast consisting of two slices of bacon, two scrambled eggs, two pieces of buttered toast with jelly, and 8 oz of whole milk. No other food or drink was given during the experimental periods.

In earlier experiments with 0.20 ppmv ozone, blood was drawn after exposure, and preexposure and postexposure urine collections were made from subjects in order to test for extrapulmonary effects of ozone. No extrapulmonary effects were found that could be attributed to ozone, but effects were found related to the order of experiments. Subjects showed stress responses related to their first exposure regardless of whether it was to ozone or to air only. In order to equalize this stress effect in later experiments, including the one reported here, blood and urine collections were made according to the same procedures as previously used.

The hypobaric chamber was kept at 72° F with a relative humidity of 10-12 percent. Ozone was generated by the action of ultraviolet light on ambient air; six ozone generators were required to attain the required concentration of ozone.

Ozone levels were monitored with an AID Model 560 ozone meter. This chemiluminescent instrument and its Model 565 calibrator were checked against a NASA Dasibi (UV absorption) instrument that was calibrated against a primary standard at the Jet Propulsion Laboratory. The AID instruments were found to agree closely with the NASA instrument. Calibration of the AID instrument was checked daily at altitude prior to experimental sessions. The output of the instrument was recorded continuously throughout experimental sessions on a strip chart recorder; variations in chamber ozone level were compensated by varying the ozone amount generated.

TABLE 1. Age-Height-Weight Characteristics of the Subject Population

	AGE (yr)	HEIGHT (cm)	WEIGHT (kg)	N
$\bar{X}$ NONSMOKERS	43.0	175.2	76.1	10
SE 40-49 YEARS	0.6	1.5	4.1	
$\bar{X}$ NONSMOKERS	54.5	179.3	84.7	10
SE 50-59 YEARS	0.9	1.9	2.2	
$\bar{X}$ NONSMOKERS	48.8	177.2	80.4	20
SE 40-59 YEARS	1.4	1.3	2.5	
$\bar{X}$ SMOKERS	44.2	176.9	78.7	10
SE 40-49 YEARS	1.0	1.8	4.2	
$\bar{X}$ SMOKERS	55.6	176.4	82.0	10
SE 50-59 YEARS	0.7	2.0	3.6	
$\bar{X}$ SMOKERS	49.9	176.7	80.3	20
SE 40-59 YEARS	1.4	1.3	2.7	
$\bar{X}$ ALL SUBJECTS	49.4	176.9	80.4	40
SE	1.0	0.9	1.8	

SECTION III

EFFECTS OF OZONE ON HEART RATE AND SHORT-TERM MEMORY

E. A. Higgins

Introduction.

The rationale for including these measurements in this study is indicated in the previous report (1). They are also included for comparing these populations representative of the flight crew with the previously studied populations.

Results.

Heart Rate.

Data for heart rate are presented in Figure 1. There were no statistically significant differences between ozone and no-ozone conditions for either smokers or nonsmokers in either age group. Also, there were no statistically significant differences when comparing smokers with nonsmokers or the 40- to 49-year-old age group with the 50- to 59-year-old age group.

Wechsler Memory Scale.

Data for the memory quotient derived from the Wechsler Memory Scale are presented in Figure 2. For this measurement there were no statistically significant differences between ozone and no-ozone conditions for either smokers or nonsmokers in either age group. Also, there were no statistically significant differences when comparing smokers with nonsmokers or the 40- to 49-year-old age group with the 50- to 59-year-old age group.

Although not pertinent to the effects of ozone, the memory quotient scores for the two groups studied this time differed from scores of the subjects of previous studies in two respects. First, for this study, there was no statistically significant difference between scores obtained in the first experiment and scores from the second administration of the test. In the prior studies, there was a significant order effect, with scores for the second test being significantly higher than for the first. Second, memory quotient scores for these two groups, both 40- to 49-year-olds and 50- to 59-year-olds, were significantly higher than for the groups previously studied. Scores for all groups are shown in Table 2.

TABLE 2. Results of Wechsler Memory Scale (in Memory Quotient Scores) for Each of the Groups Studied

Ozone Study Number	Sex	Age of Subjects (in years)	Mean Memory Quotient Score	Standard Deviation	N
1	M	21-35	118.0	± 9.1	15
1	F	21-35	117.0	± 13.0	12
2	M	21-35	115.0	± 13.5	14
2	F	21-35	116.0	± 10.4	14
3	M	21-35	122.0	± 11.6	14
3	F	21-35	120.0	± 13.4	14
4*	M	40-49	130.7	± 16.1	20
4*	M	50-59	127.4	± 19.0	20

* This study

Discussion and Conclusions.

For the two measurements reported in this section, heart rate and short-term memory, ozone had no effect when presented for 3 h at 0.30 ppmv to subjects representative of the flight crew population. Also, there were no statistically significant differences between the two age groups, 40-49 years old and 50-59 years old. Neither were there any statistically significant differences between smokers and nonsmokers.

The reason for a lack of order effect for the Wechsler Memory Scale in these older males, which was present in the younger groups studied previously, is not readily apparent. It is possible that these older men have had greater experience at the type of thinking and testing presented by the Wechsler Memory Scale than did the younger subjects. The scores for the older men were significantly higher. Further, all participants in the younger groups were paid non-FAA subjects. Thirty-six of the forty participants in these older age groups were nonpaid volunteers from the FAA's Mike Monroney Aeronautical Center and hold primarily managerial and technical positions.

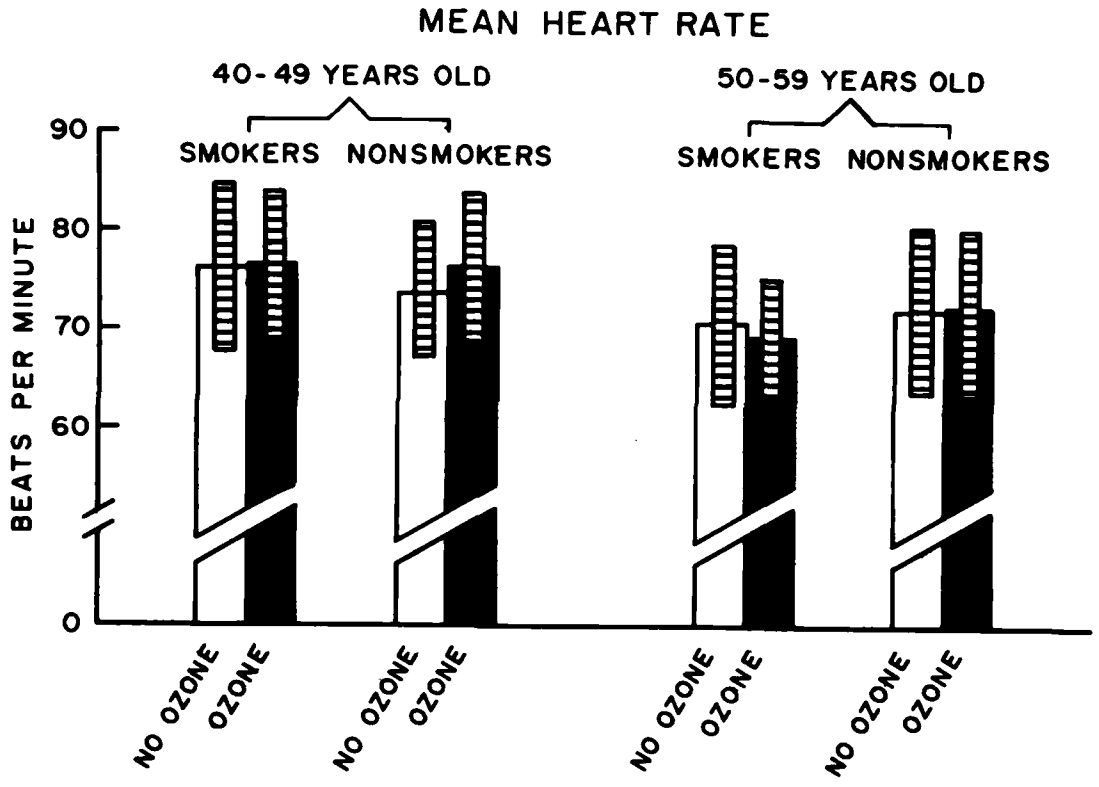


FIGURE 1. Bar graph of mean heart rate, plus or minus standard deviation, for two age groups (40- to 49-year-olds and 50- to 59-year-olds), expressed as a function of ozone exposure and no-ozone exposure for smokers and nonsmokers.

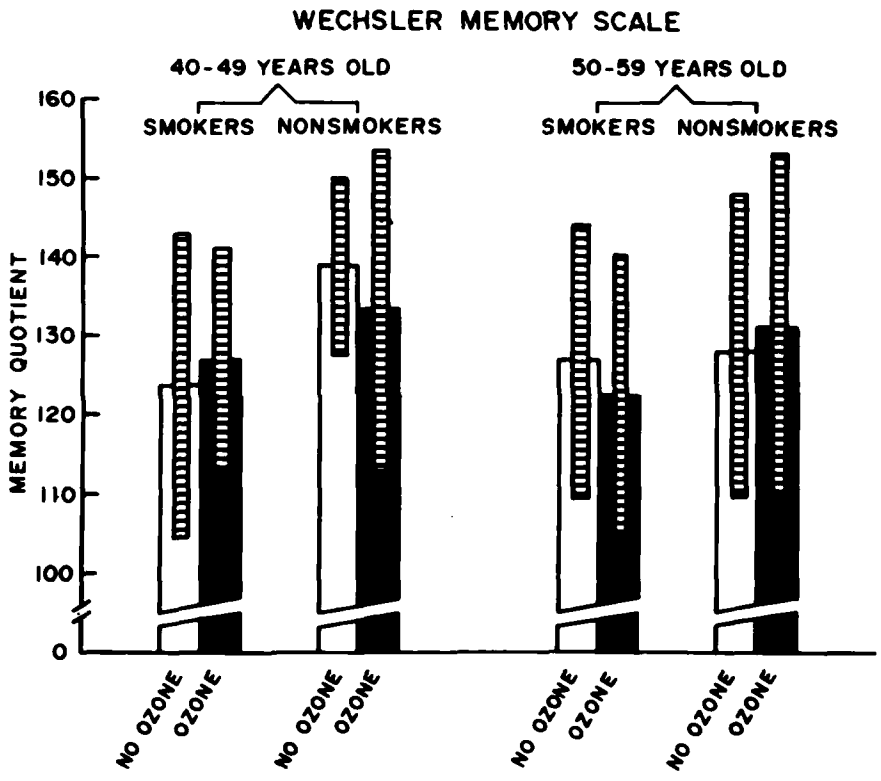


FIGURE 2. Bar graph of Wechsler Memory Scale, plus or minus standard deviation for two age groups (40- to 49-year-olds and 50- to 59-year-olds), expressed as a function of ozone exposure and no-ozone exposure for smokers and nonsmokers.

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1. Higgins, E. A., M. T. Lategola, J. M. McKenzie, C. E. Melton, and J. A. Vaughan: Effects of Ozone on Exercising and Sedentary Adult Men and Women Representative of the Flight Attendant Population, Section III: Effects of Ozone on Hand Steadiness, Heart Rate, and Short-Term Memory. FAA Office of Aviation Medicine Report No. FAA-AM-79-20, July 1979.

SECTION IV

SPIROMETRY STUDIES AND SYMPTOM QUESTIONNAIRE

M. T. Lategola

Methods.

In this study (Study 4), experimental orientation of the subjects consisted of a 45-min exposure to a chamber altitude of 6,000 ft MSL while breathing only ambient air. During this altitude exposure, each subject experienced a practice run for each test to be employed during the actual subsequent experiments. Each subject also underwent spirometric recording of at least three forced vital capacity (FVC) efforts immediately before and after the altitude orientation session. This procedure served the dual purpose of practice and additional medical screening. The subject was disqualified if postaltitude spirometric function was abnormally displaced from that of the prealtitude assessment.

After completion of the practice session, each subject who remained qualified was scheduled to return for two subsequent experiment sessions which were conducted 1 week apart.

The first procedure of the actual experiment was a symptom questionnaire. The questionnaire, which is a slight modification of one used in a previous study (5), is shown in Figure 3. This questionnaire was administered to each subject by the same person throughout all four of our ozone studies. The subject was first requested to perform one maximum-volume inspiration and expiration, and was then queried concerning the presence and degree of discomfort in each of five symptom categories as listed in Figure 1. This procedure was completely repeated by the 10th min after the subject exited the altitude chamber lock as an assessment of immediate residual effects. The subject was then asked to recall the presence and degree of discomfort in each symptom category during the whole altitude period. The numerical rating for each degree of discomfort is shown in Figure 1. The postaltitude symptomatic response was represented by the summation of the numerical differences in each symptom category between the prealtitude and postaltitude assessments. The symptomatic response for the whole altitude period was obtained by the same type of mathematical comparison with the prealtitude assessment. In this manner, each subject served as his own control in each experiment. Thus characterized, the symptomatic response of each subject in the no-ozone experiment was compared to his response in the ozone exposure experiment. Because smokers and nonsmokers were used in this study, the effect of ozone on symptoms in these two groups was assessed by comparing the ratio of the ozone/no-ozone symptomatic response of smokers to the corresponding ratio of nonsmokers.

After completing the prealtitude questionnaire, each subject underwent spirometric assessment of mechanical pulmonary function. This consisted of recording a minimum of three maximal FVC efforts using a precalibrated electronic spirometer*. During each FVC effort, the subject was seated in an upright position with a rubber nose clip in place. This FVC maneuver was conducted in accordance with a standard clinical spirometry procedure (1). The subject was allowed to rest for 1 min between maximum FVC efforts. The FVC, 1-s forced expired volume (FEV_1), FEV_1/FVC x 100 (FEV_1%), forced midexpiratory flow ($FEF_{25-75\%}$), and forced endexpiratory flows ($FEF_{50-75\%}$ and $FEF_{75-95\%}$) were selected from the data representing the best of three acceptable FVC efforts. The best effort was defined as that which yielded the largest sum of FVC + FEV_1 (11). All volumes were expressed in liters, corrected to body temperature and pressure, saturated (BTPS). The three FEF parameters were included in this assessment because of their sensitivity in detection of changes in peripheral airway resistance (3,4). Spirometric assessment was repeated immediately after the exit of each subject from the altitude chamber lock. The postaltitude FVC response of each subject was expressed as percent of his prealtitude control value (postaltitude value/prealtitude value x 100). The postaltitude responses of the other five spirometry parameters were similarly calculated and expressed. In this manner, each subject served as his own control in each experiment. Thus characterized, the spirometric responses of each subject in the no-ozone experiment were compared to his responses in the ozone exposure experiment. The effect of ozone on the spirometric responses of the smokers and nonsmokers was assessed by comparing the ratio of the ozone/no-ozone response of each spirometry parameter in the smokers to the corresponding ratio of each spirometry parameter in the nonsmokers.

Prior to ascent to altitude, three adhesive electrodes were attached to the chest of each subject for monitoring and recording a CM_5 (manubrium to V_5 plus ground) single-lead ECG (2) at altitude. The three chest electrodes were connected by shielded wires to a phone jack which was plugged into an Avionics ECG tape recorder for continuous recording of heart rate as described elsewhere in this report. A plug-in junction box, accessible within the altitude chamber, was electrically connected to a standard clinical ECG recorder located on the outside of the chamber. In the unlikely but possible event of any subjective cardiac symptoms during altitude exposure, the phone jack could be unplugged immediately from the Avionics recorder and plugged into the junction box for instantaneous monitoring and recording of the single-lead ECG. Viewing this on-line recording, an attending staff physician could decide immediately about termination or continuation of the experiment.

*Model M-10, automated spirometer, SRL Medical, Inc., Dayton, Ohio.

Independently, each subject was given the unrestricted option of terminating the experiment at any time of his choosing. Single indications for immediate termination of the equipment were inappropriate dyspnea, audible wheezing, substernal chest pain, ataxic gait, general pallor, or ECG indications of ischemia and/or arrhythmia. These cessation criteria are somewhat standard in ozone experiments of this general type (5). A staff physician and emergency resuscitation equipment were immediately available in case of need.

Results.

To compensate for any potential effects due to experimental order, half the number of males underwent the ozone exposure in the first experiment, and the remaining half underwent the ozone exposure in the second experiment. The data were pooled and compared on the basis of no-ozone versus ozone exposure.

Symptom Questionnaire.

Mean scores for subjective symptoms in the no-ozone and ozone exposure experiments are summarized in Table 3. The symptom mean scores of smokers and nonsmokers are summarized in Table 4.

As shown in Table 3, the only statistically significant ozone/no-ozone difference in symptom mean scores of the smoker group occurred in the 50- to 59-year age bracket at altitude. In the nonsmokers (Table 3), (i) both the postaltitude and altitude ozone/no-ozone differences were statistically significant in the 40- to 49-year age bracket, and (ii) the altitude ozone/no-ozone difference was statistically significant in the entire 40- to 59-year age bracket. For all subjects combined (Table 3), the ozone/no-ozone differences both at altitude and postaltitude were statistically significant. The largest ozone/no-ozone difference in symptom mean scores of the smoker groups was 7.0 and occurred at altitude in the 50- to 59-year age bracket, whereas in the nonsmoker groups the largest difference was 13.0 and occurred at altitude in the 40- to 49-year age bracket.

As shown in Table 4, none of the ozone/no-ozone symptom ratios between all smoker and nonsmoker age groups was statistically significant. Also shown in Table 4, the ozone/no-ozone symptom mean ratios of the 40- to 49-year-old nonsmoker group were larger than corresponding ratios of the 40- to 49-year-old smoker group, whereas the ozone/no-ozone symptom mean ratios of the 50- to 59-year-old nonsmoker group were smaller than corresponding ratios of the 50- to 59-year-old smoker group.

In the entire study, no experiment had to be terminated because of symptomatic stress on the part of any subject.

Spirometry.

The mean values representing displacement of all the spirometry parameters in ozone and no-ozone experiments are summarized in Table 5. The corresponding data for the comparison of the smoker and nonsmoker groups are summarized in Table 6.

As shown in Table 5, the only statistically significant ozone/no-ozone difference in the spirometry data of the smoker groups occurred in the FVC of the 40- to 49-year age bracket. In the nonsmoker groups (Table 5), statistically significant displacements occurred in the ozone/no-ozone differences; (i) in the FVC of the 40- to 49-year age bracket, (ii) in the FVC and $FEF_{75-95\%}$ of the 50- to 59-year age bracket, and (iii) in the FVC and FEV_1, of the 40- to 59-year age bracket. For all smokers and nonsmokers combined (Table 5), statistically significant displacements occurred in the ozone/no-ozone differences of the FVC, FEV_1, and $FEF_{75-95\%}$. The relatively few ozone/no-ozone differences that were statistically significant were somewhat small in magnitude with a range of 1.3-8.9 percent. Directionally, ozone exposure decreased the bulk of the spirometric mean values relative to the commensurate no-ozone values (Table 5).

As shown in Table 6, none of the ozone/no-ozone spirometric ratio differences between all the smoker and nonsmoker groups was statistically significant.

Discussion and Summary.

Symptom Questionnaire.

As shown previously in Table 3, all smokers and nonsmokers combined manifested small but statistically significant displacements of symptoms associated with ozone exposure. These total-group displacements were due mainly to larger symptomatic displacements in the 40- to 49-year-old nonsmokers both at altitude and postaltitude, and in the 50- to 59-year-old smokers only at altitude. The largest symptom mean score of 16.0 in the 40- to 49-year-old nonsmokers lies between "slight" and "moderate" according to the symptom rating scale shown in Figure 3.

In four ozone studies conducted to date at altitude (Studies 1 and 2 with treadmill exercise included, and Studies 3 and 4 under sedentary conditions only) (7), the bulk of the symptom mean scores of ozone exposure at altitude were greater than those occurring approximately 20 min after cessation of the ozone exposure at the postaltitude time of symptom assessment. This generally corroborates a previous observation (8) that recovery from completely reversible degrees of ozone symptoms occurs somewhat rapidly after cessation of ozone exposure.

In our preceding study (Study 3) of sedentary exposure of younger nonsmoking male subjects (mean age of 25.2 years) to ozone at altitude (7), the largest symptom mean score of 11.4 occurred at altitude, and

approached statistical significance ($p = 0.056$) when compared with the corresponding symptom mean score of the no-ozone exposure.

As reflected in Table 4, no statistically significant differences occurred in the ozone/no-ozone symptom mean ratios between the smoker and nonsmoker groups. Although the ozone/no-ozone symptom mean ratios of all nonsmokers combined were greater than the corresponding values for all the smokers combined, the direction of these data was the same in the 40- to 49-year age bracket, but was reversed in the 50- to 59-year age bracket (Table 4). Two previous studies (6,9) have reported that symptomatic response to single ozone exposures was greater in nonsmokers than in smokers. In both these studies (6,9) the subjects were 10 to 20 years younger than in our current study. The ozone concentrations were greater (0.37-0.75 ppmv), and the duration of the exposure in one of the two studies (9) was twice as long as in ours.

In our study, the twenty participating smokers had smoked an average of 30 to 35 pack years (1 pack year = one pack of cigarettes per day x 1 year). The nonsmoker group contained 12 subjects who had never smoked, and 8 who had substantial smoking histories but currently had not smoked for 0.5 to 20 years. Conjecturally, it is possible that smoking histories of those in the nonsmoker group may have contributed some of the directional variability seen in Table 4.

With only three exceptions, all reported ozone symptoms had disappeared within 4 hours after the cessation of ozone exposure. One 40-year-old smoker reported an irritated throat and cough lasting 8 hours, and two others (one smoker and one nonsmoker) complained of unusual fatigue which lasted the remainder of the day. All ozone symptoms generated in this study appear to have been completely reversible.

Eye discomfort was the most prevalent ozone symptom reported in this study. In descending order, headache, nasal irritation, and throat irritation were the next most prevalent symptoms. This same order of symptom prevalence also occurred in our third identically conducted study using younger male subjects (mean age of 25.2 years). The primary prevalence of eye discomfort in these two studies (Studies 3 and 4) is in contrast with the more prevalent throat and substernal symptoms occurring in our second ozone study. This apparent discrepancy in the primary symptom prevalence is probably explained by two differences in the experimental protocol. Although the duration of exposure to 0.3 ppmv ozone at altitude was identical in Studies 2, 3, and 4, the presence of three treadmill tests in Study 2 and none in Studies 3 and 4 may have accentuated throat and substernal symptoms in Study 2 because of the substantial increase in oral ventilation occurring during the treadmill tests. The occurrence of eye testing toward the end of the 3-h altitude/ozone exposure in Studies 3 and 4, and towards the beginning of the altitude/ozone exposure in Study 2, may have accentuated eye irritation in Studies 3 and 4 as a function of the greater duration of ozone exposure preceding the eye tests. The greater prevalence of nasal irritation in Studies 3 and 4 as compared with Study 2 (7) may have resulted from relatively more

nasal breathing in Studies 3 and 4. Under the essentially sedentary conditions of Studies 3 and 4, nasal breathing would have a greater probability of occurring than either oronasal or oral breathing. If nasal breathing did predominate in Studies 3 and 4, it could explain some of the diminution of thoracic symptoms and spirometric displacements of Studies 3 and 4 as compared to Study 2. The presence of nasal scrubbing of ozone (12,13) may have actually reduced the intrapulmonic exposure to ozone in Studies 3 and 4, whereas the nonoptional switch from nasal to increased oral breathing during the treadmill tests of Study 2 may have relatively accentuated the intrapulmonic exposure to ozone. If generally true, this deduction suggests that, in the presence of an unavoidable exposure to ozone, some degree of intrapulmonic protection might be afforded by breathing only through the nose. This temporary expedience may have increased significance for individuals who may have increased intrapulmonic sensitivity to ozone due to such conditions as asthmatic allergies.

The fact that qualitative differences between the ozone and no-ozone symptom mean scores did occur in this study, and that some of those differences reached statistical significance, most probably means that a 3-h exposure of older males (40 to 59 years) to 0.3 ppmv ozone at altitude under essentially sedentary conditions is right at the threshold of symptomatic effects of ozone.

Spirometry.

As shown in Table 5, all smokers and nonsmokers combined manifested small but statistically significant ozone/no-ozone differences in FVC, FEV_1, and $FEF_{75-95\%}$. With only one exception within the smoker groups, the statistically significant spirometric differences of all subjects combined were due to those occurring within the nonsmoker groups (Table 5). In the nonsmoking younger males (mean age of 25.2 years) of Study 3 (7), only one spirometric parameter ($FEF_{50-75\%}$) manifested a statistically significant ozone/no-ozone difference.

The fact that some small but statistically significant ozone/no-ozone spirometric differences did occur in Study 4 probably means that a 3-h exposure to 0.3 ppmv ozone at altitude under somewhat sedentary conditions is right at the threshold (10) for spirometric effects of ozone.

As shown in Table 6, none of the smoker/nonsmoker differences in the ozone/no-ozone spirometric ratios were statistically significant. A qualitative trend of greater ozone/no-ozone decreases in the smokers, as compared to nonsmokers, was not apparent in the mean values of Table 6. This probably means that the experimental conditions of ozone exposure used in Study 4 were insufficient to reach the threshold of separation for smokers versus nonsmokers. That such a threshold exists is evidenced in two other studies (6,9) which compared smokers' and nonsmokers' responses to greater ozone concentrations, longer durations, and intermittent exercise. In those studies

(6,9), ozone concentrations of 0.5 ppmv and 0.75 ppmv clearly and significantly displaced the spirometric functions of smokers more than those of nonsmokers. The statistically significant separation of smokers' versus nonsmokers' spirometric decrements did not occur until the second hour of ozone exposure. In one of those studies (6), the greater decrements in spirometric function which occurred in the smokers after a 2-h exposure to 0.75 ppmv ozone were paradoxically accompanied by symptomatic displacements, which were much less than the corresponding symptomatic displacements of the nonsmokers. If generally true, this dissociation of symptomatic and spirometric responses in smokers could make the smokers more vulnerable than the nonsmokers to intrapulmonic ozone damage, because of the diminution or absence of symptomatic warnings during unexpected ozone exposure.

Summary.

Under essentially sedentary conditions of altitude exposure (6,000 ft MSL), the threshold for reversible adverse effects of ozone on subjective symptoms and objective spirometric function in 40- to 59-year-old men appears to be right at a 3-h exposure to 0.3 ppmv. Populationwise, this would be relevant to sedentary male passengers and cockpit aircrew. The general disappearance of ozone symptoms within 4 h of cessation of experimental ozone exposure probably implies that such displacements due to a single exposure of 0.3 ppmv ozone for a 3-h duration are completely reversible. The symptoms and spirometric functions of the smokers as compared to nonsmokers did not manifest statistically significant differences. The symptom data of this study strengthened a tentative deduction from Studies 2 and 3 that, in the presence of unavoidable exposure to ozone, some degree of intrapulmonic protection might be afforded by breathing only through the nose.

TABLE 3. Subjective Symptom Scores

Ozone Versus No-Ozone

		(Postaltitude)-(Prealtitude)			(Altitude)-(Prealtitude)		
		Ozone		No-Ozone	Ozone		No-Ozone
(1) S	$\bar{X}$	4.0		1.0	3.0		3.5
	SE	2.1		1.0	1.5		1.8
(2) S	$\bar{X}$	2.5		0.5	9.0	*	2.0
	SE	1.1		0.5	2.8		1.3
(3) S	$\bar{X}$	3.3		0.8	6.0		2.8
	SE	1.2		0.6	1.7		1.1
(1) NS	$\bar{X}$	10.5	*	1.0	16.0	**	3.0
	SE	4.0		1.0	4.2		1.5
(2) NS	$\bar{X}$	2.0		3.5	7.0		6.0
	SE	1.3		2.1	3.7		2.7
(3) NS	$\bar{X}$	6.3		2.3	11.5	*	4.5
	SE	2.3		1.2	2.9		1.5
ALL	$\bar{X}$	4.8	*	1.5	8.8	**	3.6
	SE	1.3		0.7	1.7		0.9

$\bar{X}$ = mean. SE = standard error of the mean.
S = smoker NS = nonsmoker
(1) = 40-49 years
(2) = 50-59 years
(3) = 40-59 years
* = Statistically significant difference ($p \leq 0.05$)
** = Statistically significant difference ($p \leq 0.01$)

TABLE 4. Subjective Symptom Scores

Smokers Versus Nonsmokers

$$\frac{\text{Ozone: (Postaltitude)-(Prealtitude)}}{\text{No-Ozone: (Postaltitude)-(Prealtitude)}} \times 100 \qquad \frac{\text{Ozone: (Altitude)-(Prealtitude)}}{\text{No-Ozone: (Altitude)-(Prealtitude)}} \times 100$$

(1) S $\bar{X}$	451	262
(1) S SE	197.7	123.6
(1) NS $\bar{X}$	955	1090
(1) NS SE	400.6	450.5
(2) S $\bar{X}$	270	841
(2) S SE	96.7	278.2
(2) NS $\bar{X}$	254	292
(2) NS SE	125.1	191.5
(3) S $\bar{X}$	360	551
(3) S SE	109.1	162.4
(3) NS $\bar{X}$	604	691
(3) NS SE	219.5	255.2

$\bar{X}$ = mean. SE = standard error of the mean.
S = smoker NS = nonsmoker
(1) = 40-49 years
(2) = 50-59 years
(3) = 40-59 years

TABLE 5. Spirometry Data, Ozone Versus No-Ozone

$$\frac{\text{Postaltitude Value}}{\text{Prealtitude Value}} \times 100$$

	FVC	FEV_1	$FEV_1/FVC \times 100$	FEF 25-75%	FEF 50-75%	FEF 75-95%
(1) Ozone $\bar{X}$	98.3*	98.7	100.4	102.0	102.2	103.3
SE	1.1	0.9	0.4	0.8	1.4	1.2
(1)No-Ozone $\bar{X}$	101.8	101.3	99.6	102.6	102.7	104.1
SE	1.0	1.1	0.5	1.9	2.2	2.4
(2) Ozone $\bar{X}$	99.8*	99.6	99.7	98.0	96.8	93.0*
SE	0.3	0.6	0.6	2.4	2.4	2.0
(2)No-Ozone $\bar{X}$	101.1	101.4	100.3	103.1	103.4	101.9
SE	0.4	0.7	0.5	2.4	2.2	3.2
(3) Ozone $\bar{X}$	99.1**	99.2**	100.1	100.0	99.5	98.2
SE	0.6	0.5	0.3	1.3	1.5	1.6
(3)No-Ozone $\bar{X}$	101.5	101.4	100.0	102.9	103.1	103.0
SE	0.6	0.6	0.4	1.5	1.5	2.0
(4) Ozone $\bar{X}$	97.9*	98.4	100.5	98.9	99.1	93.6
SE	0.6	0.8	0.5	1.5	1.2	2.6
(4)No-Ozone $\bar{X}$	100.1	100.3	100.2	101.0	101.9	97.5
SE	0.6	0.6	0.5	1.1	1.0	1.8
(5) Ozone $\bar{X}$	100.4	100.6	100.2	101.7	101.7	88.9
SE	1.1	1.9	0.8	4.3	6.0	4.2
(5)No-Ozone $\bar{X}$	100.7	102.4	101.6	107.0	108.8	97.4
SE	1.3	2.1	0.8	4.6	5.2	4.5
(6) Ozone $\bar{X}$	99.2	99.5	100.4	100.3	100.4	91.3
SE	0.7	1.0	0.5	2.2	3.0	2.5
(6)No-Ozone $\bar{X}$	100.4	101.4	100.9	104.0	105.4	97.5
SE	0.7	1.1	0.5	2.4	2.7	2.3
(7) Ozone $\bar{X}$	99.2**	99.4*	100.3	100.2	100.0	94.8*
SE	0.4	0.6	0.3	1.3	1.7	1.5
(7)No-Ozone $\bar{X}$	101.0	101.4	100.5	103.5	104.3	100.3
SE	0.5	0.6	0.3	1.4	1.5	1.6

(1) = Nonsmokers, 40-49 years old
(2) = Nonsmokers, 50-59 years old
(3) = Nonsmokers, 40-59 years old
(4) = Smokers, 40-49 years old
(5) = Smokers, 50-59 years old
(6) = Smokers, 40-59 years old
(7) = Smokers and Nonsmokers, 40-59 years old
* = Statistically significant difference ($p \leq 0.05$)
** = Statistically significant difference ($p \leq 0.01$)

TABLE 6. Spirometry Data

Smokers Versus Nonsmokers

$$\frac{\text{Ozone: } \frac{\text{Postaltitude Value}}{\text{Prealtitude Value}}}{\text{No-Ozone: } \frac{\text{Postaltitude Value}}{\text{Prealtitude Value}}} \times 100$$

		FVC	FEV_1	$FEV_1/FVC \times 100$	FEF 25-75%	FEF 50-75%	FEF 75-95%
(1) S	$\bar{X}$	97.8	98.2	100.4	97.9	97.3	95.9
	SE	0.8	0.7	0.5	0.7	1.1	1.3
(1) NS	$\bar{X}$	97.6	97.5	100.9	99.7	99.8	99.6
	SE	1.6	1.5	0.6	2.0	2.3	2.3
(2) S	$\bar{X}$	99.8	98.4	98.6	95.3	93.4	91.6
	SE	0.4	0.6	0.5	2.2	2.5	2.6
(2) NS	$\bar{X}$	99.0	98.2	99.4	95.2	93.7	91.8
	SE	0.4	0.4	0.3	1.7	1.7	2.4
(3) S	$\bar{X}$	98.4	98.1	99.9	97.1	96.1	94.8
	SE	0.5	0.4	0.3	0.9	1.1	1.2
(3) NS	$\bar{X}$	97.9	97.9	100.2	97.5	96.8	95.7
	SE	0.9	0.8	0.4	1.4	1.6	1.9

$\bar{X}$ = mean. SE = standard error of the mean.
S = smoker NS = nonsmoker
(1) = 40-49 years
(2) = 50-59 years
(3) = 40-59 years

SUBJECT #_____ A B INITIALS _____ DATE _____ OZONE_____ NO-OZONE_____

SYMPTOM CHECKLIST	PREALTITUDE	ALTITUDE	POSTALTITUDE

DISCOMFORT IN:

1. Throat
2. Under Breastbone
3. Chest (Other Than #2)
4. Headache
5. Other

RATINGS FOR DEGREE OF SYMPTOMATIC DISCOMFORT:

0 = None. 5 = Trace = Unsure of presence of discomfort.

10 = Slight = Symptom present but not annoying.

20 = Moderate = Symptom present and annoying

30 = Severe = Symptom present and clearly painful.

FIGURE 3. Symptom questionnaire

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SECTION V

THE EFFECTS OF OZONE ON PHOTOPIC, MESOPIC, AND SCOTOPIC VISION

J. A. Vaughan

Introduction.

The assessment of the possibility of impaired vision caused by the exposure of human test subjects to ozone was determined by a battery of 12 vision tests conducted when the subjects were light adapted (photopic vision), twilight or semidark adapted (mesopic vision), or dark adapted (scotopic vision). The following tests were given for each of the above illumination categories: Photopic vision included tests for distant visual acuity, stereoscopic acuity, vertical and lateral phorias, accommodation, hand-eye coordination, color vision, and blink rate; mesopic vision tests consisted of determinations of visual fields and retinal bleach recovery; and scotopic vision was assessed by dark adaptation and numerical recognition.

The purpose of this experiment was to compare the effects on vision of male test subjects in room air (no-ozone) to those experienced at an ozone concentration of 0.30 ppmv, both at a simulated altitude of 6,000 ft.

Methods.

The 40 male test subjects were separated equally into two age groups of 40 to 49 years and 50 to 59 years. Each age group of 20 subjects was further separated into 10 smokers and 10 nonsmokers. All of the test subjects were examined for normal distant visual acuity, near visual acuity, and stereoscopic acuity before being selected for the experiment, and wore corrective lenses when required for good vision during the two exposure periods. In the 40- to 49-year age group, six subjects (30 percent) needed no prescription lenses, six (30 percent) wore spherical corrective lenses, seven (35 percent) wore bifocals, and one subject (5 percent) wore contact lenses. In the 50- to 59-year age group, all the subjects wore corrective lenses, of which four (20 percent) were spherical, 14 (70 percent) were bifocals, and two (10 percent) were trifocal lenses.

Photopic Vision.

The Titmus Vision Tester was employed to determine the parameters of distant visual acuity for each eye (slides ARF-1 and ALF-1), stereoscopic acuity (slide SDF-1), vertical phoria (slide VPF-1), and lateral phoria (slide LPF-1). Accommodation was measured with the Royal Air Force Near Point Rule, using techniques of "out-to-clear" and "in-to-blur." Color vision was determined with the Farnsworth Panel D-15 Color Test. The hand-eye coordination task consisted of an "Etch-a-Sketch" with a design consisting of two parallel lines drawn on a clear plastic overlay. The subject was required to "draw" a line between the limiting lines on the overlay. The procedure was timed with a stopwatch and errors were recorded on a Polaroid photograph. Measurements

of blink rate were made by an outside observer looking into the altitude chamber through a one-way glass temporarily positioned over the window. One observer counted the eyeblinks with a laboratory counter while a second observer timed the procedure for 1 min with a stopwatch. Four 1-min counts were made by the same observer on each subject; means and ranges were calculated later.

Mesopic Vision.

The bleach recovery test was conducted using the numbers with the visual acuity fraction of 20/60 (2.5-mm height) on the slide. The observer occluded the test numbers and set the test light at 5.5 (on a scale of 7.0) log units, and the test subject again positioned his head on the chinrest. The bleaching lights (700 fL) were turned on for 3 min; immediately following the bleach, the observer simultaneously removed the occluder and started a stopwatch. Bleach recovery time was the number of seconds required for the subject to read the numbers correctly.

Visual fields were determined under mesopic vision conditions (chamber lights out but windows uncovered) with the Harrington-Flocks Multiple Pattern Visual Field Screener (Model B-11). Errors were recorded for 10 presentations to each eye.

Scotopic Vision - Dark Adaptation.

After the subjects were given a final briefing, the overhead lights were extinguished. Each subject positioned his head on the chinrest of the light chamber of the Goldmann-Weekers Adaptometer (Haag-Streit) with the test aperture occluded, and two 60W bleaching lights reflecting 700 fL were turned on for a period of 3 min. Immediately after the lights were turned off, the subject donned a pair of opaque goggles and wore them for the next 25 min. The subject then took off the goggles and repositioned his head on the chinrest. For each scotopic vision test, a black velvet cloth was draped around the subject's head and shoulders to exclude any ambient light. The subject was asked to gaze at a dim, red fixation light about 11° above the test plate mounted in the aperture. The test plate, 5.5 cm in diameter, consisted of alternating black and white bars (100 percent contrast). The black bars were opaque but the translucent white bars transmitted 49 percent of the light and were blacklighted by a 9W test lamp. The intensity was controlled by the observer, from 0 to 10 mL as calibrated with the Pritchard Spectra Photometer, Model 1970-PR. The illumination intensity of the test light was synchronized with a mechanically linked recording arm and stylus that traveled vertically along the ordinate of a chart attached to a rotating drum. With the test light turned to its lowest position (no light), the observer signaled "ready" and slowly increased the illumination with the test light. The test subject tapped the instant he could identify the orientation of the bars (horizontal, vertical, or oblique), and the observer perforated the chart with the stylus at that point. The observer then changed the orientation of the bars and the procedure

was repeated twice more within the 2-min period. The subject was then allowed to remove his head from the apparatus for 6 min, and three more consecutive measurements were taken in a second 2-min period. This modified procedure replaced the usual method of measuring dark adaptation (taking a point at 1- or 2-min intervals) because trial runs demonstrated a large decrease in ozone concentration breathed by the subject with his head in the adaptometer during the first 30 min, whereas ozone concentration decrements were small during the two 2-min test periods.

During the numerical recognition test, the subject maintained scotopic vision while the observer removed the bar test plate and positioned a plastic visual acuity slide on the adaptometer. The slide contained six groups of numbers in graded sizes, of which only four groups were used. Each group contained three two-digit numbers. Heights of the numbers were 1.0 mm, 1.5 mm, 2.5 mm, and 4.5 mm, with visual acuity equivalents of 20/25, 20/35, 20/60, and 20/105, respectively, after correction for viewing distance of 30 cm recommended for the adaptometer (3). With the occluder in place, the test light at the lowest position and the subject's head on the chinrest, the observer removed the occluder and slowly increased the target illumination until the subject again signaled "stop," and identified the six numbers. As before, the subject repeated the procedure until the four groups of numbers were read.

Statistical analysis of the data consisted of an analysis of variance for a three-factor experiment with repeated measures. Statistically significant interactions were further tested by analysis on interactions between variables using the simple effect method (10).

Results.

Photopic Vision.

Visual acuity. The effects of ozone on distant visual acuity, in terms of the Snellen fraction, are presented in Table 7. Corrected vision was significantly poorer in the older age group, but there were no differences in visual acuity that could be attributed to the effects of ozone or to smoking habits. Sixty percent of the test subjects in the 40- to 49-year age group and 45 percent of the subjects in the 50- to 59-year age group maintained visual acuities of 20/20 or better (20/13 to 20/20) for a total of 21 subjects, or 52.5 percent in the complete sample.

Stereoscopic acuity. Results of the analysis of variance for stereoscopic acuity showed no significant changes with age, smoking habits, or ozone (Table 8). During preexposure examination, each subject was tested for stereopsis with a Titmus Vision Tester and the Titmus book test, both of which presented characters identical with those of the Titmus Vision Tester used during the two actual exposures.

Vertical and lateral phorias. The numbers and percentages of test subjects in the two age groups which showed effects of ozone on vertical and lateral phorias are presented in Table 9. Changes in vertical phorias were small, ranging from 0.00 to 1.00 Prism Diopters (PD), and a high percentage showed no changes at all. In the total sample, 13 subjects (32.5 percent) had left hyperphoria, and 4 subjects (10 percent) showed right hyperphoria in one or both exposures. Twenty-three subjects (57.5 percent) demonstrated vertical orthophoria during both exposures.

The range of values for lateral phorias was 0.00 to 6.00 PD. Lateral phorias were somewhat improved in some of the smokers and nonsmokers of the 40- to 49-year age group and in the nonsmokers of the 50- to 59-year age group; but, as with the vertical phorias, the majority of the test subjects showed no change from no-ozone to ozone conditions. In the younger age group, eight subjects (40 percent) had esophoria and five subjects (25 percent) exophoria during one or both exposures. The older age group showed 7 subjects (35 percent) with esophoria and 11 subjects (55 percent) with exophoria during one or both exposures.

Accommodation. Mean values of accommodation measured with the R.A.F. Near Point Rule are shown in Table 10. There was a significant increase in the number of centimeters necessary to read in the "out-to-clear" procedure between no-ozone and ozone ($p \leq .01$), but not for the age groups or between smokers and nonsmokers. No significant differences were found when the "in-to-blur" procedure was employed.

Farnsworth Panel D-15 color test. Results of this test, shown in Table 11, indicate no effects of exposure to ozone on color discrimination, and all subjects were error-free in choosing the correct hues. Individual times taken to complete the test ranged from 24 s to 79 s. The 50- to 59-year age group showed a trend toward longer completion time, with a similar trend for smokers, but no true cause-and-effect relationships could be demonstrated statistically.

Hand-eye coordination. The time to complete the hand-eye coordination test using the "Etch-a-Sketch" device, together with errors made, is shown in Table 12. Completion times ranged from 52 to 182 s in the 40- to 49-year group, and from 61 to 193 s in the 50- to 59-year age group. The older group decidedly used more time to complete the test ($p \leq .01$), but mean errors did not exceed those of the 40- to 49-year age group. There were no significant differences found due to exposure to ozone or to the smokers for either completion time or number of errors accrued.

Blink rate and range. Changes in mean blink rates and ranges are presented in Table 13. The data reveal a highly significant increase in blink rate from no-ozone to ozone exposures ($p \leq .01$) and an interaction between the ozone exposures and the smoking and nonsmoking conditions ($p \leq .05$). Further analysis on interactions between variables using the test for simple effects (10) indicated that for nonsmokers there

was a significant increase in blink rate ($p \leq .01$) from no-ozone to ozone, but not for smokers, and a significant decrease from smokers to nonsmokers ($p \leq .01$) in the no-ozone condition but not with ozone. There were no significant differences for smokers between no-ozone and ozone. Analysis of the ranges of the four blink rates measured at each exposure showed significant decreases between smokers and nonsmokers ($p \leq .05$) but with no significant interactions or differences caused by smokers or the ozone concentration. Mean blink rates ranged from 4.0 B/min to 42.8 B/min (the latter in subject No. 05, who wore contact lenses, demonstrating the largest range of 18 B/min). The smallest range in blink rates was 1 (4 to 5 B/min) by subject No. 32.

Mesopic Vision.

Visual fields. Values measured with the Harrington-Flocks Screener are summarized in Table 14 in terms of numbers of subjects and percentage change from no-ozone. Analysis of variance revealed no significant differences between no-ozone and ozone, or between smokers and nonsmokers. There was a significant increase in number of errors made by the 50- to 59-year age group over the 40- to 49-year age group ($F = 4.90$, $p \leq .05$). The increase in mean errors indicates a loss in visual fields that is attributed to the presbyopic eye, but not to ozone. Forty to sixty percent of the test subjects showed no changes in visual field from the conditions of no-ozone to ozone.

Retinal bleach recovery time. The time required for the subject to correctly identify two-digit numbers at 20/60 visual acuity under dim illumination following a 3-min bleach is presented in Table 15. There was a significant overall increase in recovery time ($p \leq .05$) from the no-ozone to ozone exposures, but no effects were found which could be traced to age or smoking habits. As shown by the standard deviations, bleach recovery times were highly variable and individual values ranged from 19 to 300 s. The levels of ozone concentration of this study apparently delayed the neurochemical recovery of the bleached retina to a considerable extent.

Scotopic Vision.

Scotopic visual acuity. The values of Table 16 indicate the mean responses to light energy after about one-half hour in total darkness, and quantify the levels of dark adaptation under these conditions. The overall light energy was significantly higher ($p \leq .05$) for subjects exposed to ozone than with no-ozone. Further analysis (10) using the simple effects test indicated an interaction between no-ozone and ozone for smokers ($p < .01$) but not for nonsmokers. There was also an interaction of an increase in light energy with ozone for smokers of the 50- to 59-year age group ($p < .01$). There is evidence from the data, then, that ozone does inhibit the process of dark adaptation.

Numerical recognition. The means and standard deviations of the light energy required for dark-adapted subjects to read four sizes of two-digit numbers are shown in Table 17. Values are significantly

different only for the largest numerals (20/105) and show an overall increase in light energy with ozone ($p \leq .05$). The interaction between the ozone condition and smoking habits is barely significant at $p \leq .05$ and the analysis by the Simple Effects procedure (10) revealed no significant differences among the separate variables of smokers, nonsmokers, no-ozone, or ozone. The significant result found (for the 20/105 column) and the interaction were probably caused by distribution of the data, because the larger numerals are more easily seen and results are more uniform.

Subjective Questionnaire.

At the postexposure debriefing sessions, 10 test subjects reported burning and/or watering eyes during exposure to 0.30 ppmv of ozone. In the 40- to 49-year age group, one smoker and two nonsmokers complained of slight to moderate burning eyes. No watering eyes were reported for this age group. In the 50- to 59-year age group, seven smokers and three nonsmokers reported slight to moderate burning or watering of the eyes during exposure to ozone, but only one subject reported watering in the no-ozone environment.

Discussion.

Analysis of variance revealed some differences in the vision parameters examined in this experiment attributable to ozone. Lagerwerff (6) also investigated several visual functions in an atmosphere of ozone. Although methods differed, his results agree with those of this study in that photopic distant visual acuity, stereoscopic acuity, vertical phoria, and color vision were not significantly influenced by by a 3-h exposure to 0.30 ppmv of ozone. The data in Table 7 show a small but significant increase in the Snellen Fraction between the age groups; the 50- to 59-year age group had slightly poorer vision, which can be attributed to presbyopia. The optical differences are slight and have no practical meaning. The hand-eye coordination test was also not affected during exposure to ozone (Table 12). In each condition the older age group took more time to complete the test than the younger age group, but made about the same number of errors.

Lagerwerff did report a sizable decrease in scotopic vision with ozone. The values in Table 16 also show that a higher threshold of dark adaptation occurs when the subjects are exposed to ozone. However, further analysis of the interactions between variables reveal that this significant increase is caused by the smokers in the 50- to 59-year age group only ($p < .01$) but not for the remaining variables. Increase in visual threshold here is not caused exclusively by ozone, but is a factor of age and smoking habits. An earlier study with conditions identical to this study but with younger test subjects revealed on significant differences in dark adaptation with ozone (4). Fourteen male test subjects from that study (age 20 to 33 years) were compared with the 20 older subjects (50 to 59 years) of this study (Table 16). In the

younger age group, the mean visual threshold in terms of light energy for scotopic vision with no-ozone was 0.46 μL compared with 0.54 μL in the older age group of Table 16. With ozone, the mean threshold was 0.57 μL for the younger group and 0.72 μL for the older group. Mean light energy values for the 40- to 49-year age group were 0.46 μL and 0.50 μL, and were similar to those of the 20- to 33-year group of the previous study. Adler (1) states that scotopic vision begins at approximately 1.0 μL and is in effect with increasing illumination up to 550 μL. The data of this report are well within that range, and the subjects may be considered to be dark adapted.

McFarland attributes the limitations in dark adaptation in older subjects to an interference of normal metabolic processes within individual nerve cells of the brain and retina. This interference may operate through a reduced rate of transfer of essential substances required for normal metabolic processes (7). The reason why smokers in the older age group showed changes with ozone is not clear. Impairment of night vision by the byproducts of smoking (e.g., carbon monoxide) is generally accepted, and the presence of ozone may be additive and responsible for the increase in the final threshold levels for vision in older subjects.

Lagerwerff also reported that 76.9 percent of his subjects demonstrated a net increase in peripheral vision in an ozone concentration of 0.35 ppmv during a 3-h exposure period (6). Values of visual fields of this study shown in Table 14 do not agree with Lagerwerff's results. The only categories that showed an increase in visual fields with ozone was the left eyes of the smokers in the 50- to 59-year age group and the nonsmokers in the 40- to 49-year age group. Forty to sixty percent of the subjects showed no change in visual fields with ozone, as measured with the Harrington-Flocks Screener.

The mechanism for the differences in the near point of accommodation between the "in-to-blur" and the "out-to-clear" procedures is not clear (Table 10). Paired t tests between the two procedures for the subjects in the ozone condition were not statistically significant in either the 40- to 49-year age group or the 50- to 59-year age group. Armstrong (2) describes the "out-to-clear" procedure as part of the examination for prospective pilots using Prince's rule, but offers no further information; data are also lacking in the general literature on the subject. The causes are not part of the convergence-accommodation controlled at the higher neurological centers because measurements were monocular, in which mechanisms involving nuclei of the third cranial nerve do not apply. Whatever the mechanism, it is probable that the response is not associated with ozone exposure.

An increase in the rate of eye blinks is a symptom of eye irritation from one source or another. Study of the data in Table 13 indicates a significant increase in blink rate ($p \leq .01$) when subjects are exposed

to ozone. Additional analysis of the interaction reveals that this increase is accounted for by the nonsmokers ($p \leq .01$). There were no differences in smokers between no-ozone and ozone conditions. During no-ozone exposure, the nonsmokers had a significantly lower blink rate and range ($p \leq .01$ and $p \leq .05$ respectively) than the smokers, so that a rise in rate was more readily attained by the nonsmokers. Since the smokers were not permitted to smoke for about 1 hour before exposure, or during exposure, and differences in blink rate between smokers and nonsmokers were not observed with ozone, no explanation of the mechanism to this result can be given here. Six smokers and four nonsmokers reported burning or watering eyes during exposure to ozone. Only one subject (a smoker) reported burning eyes during the no-ozone exposure. These subjective symptoms of eye irritation could have influenced, to some degree, the higher blink rates observed with ozone. Eye irritation symptoms were not severe and cleared up following exposure. Subjective symptoms of irritation to the eyes and respiratory tract have been reported for ozone concentrations in air greater than 1 ppmv, and concentrations of 2.0 to 3.7 ppmv have caused irritation to normal human eyes within 6 min (5). At concentrations that are irritating to human eyes, ozone was demonstrated not to be injurious to corneas of experimental animals. Exposure of rabbits to 2.0 to 2.8 ppm for 4 hours daily over a period of 1 to 25 days caused no injury to the corneas, as detected by clinical examination, by measurement of rate of repair of artificial epithelial wounds, by histological methods, or by measurement of the activity of several enzymes in the epithelium (5,8,9).

Summary.

Statistical analysis of the results indicated that a 3-h exposure to 0.30 ppmv of ozone caused only minor effects on the visual parameters of photopic distant visual acuity, stereoscopic acuity, vertical and lateral phorias, color vision, hand-eye coordination, and peripheral visual fields. Visual impairment in accommodation was found with ozone when measured by the "out-to-clear" procedure. Visual threshold during dark adaptation was higher with ozone and with the older (50- to 59-year) age group who were nonsmokers, but numerical recognition was higher in the dark-adapted subjects exposed to ozone only when viewing the largest size numerals. Retinal bleach recovery times were also significantly increased during exposure to ozone. The significantly higher blink rates, together with subjective reports of tearing and slight to moderate burning in the eyes of 25 percent of the test subjects, indicated ozone to be a temporary irritant which possibly contributed to degradation of scotopic vision, accommodation, and elevated retinal bleach recovery times at the ozone concentration examined in this study.

TABLE 7. Photopic Distant Visual Acuity

AGE (yr)	NO-OZONE				OZONE			
	Smokers		Nonsmokers		Smokers		Nonsmokers	
	Snellen Fraction				Snellen Fraction			
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
40 to 49	20/22.4	20/5.6	20/19.8	20/7.4	20/22.7	20/5.3	20/19.3	20/3.0
50 to 59	20/25.0	20/9.0	20/27.2	20/10.3	20/26.0	20/7.9	20/27.8	20/10.2

F-Ratios: Age Groups $F = 6.09$ ($p \leq .05$)

Smokers and Nonsmokers $F = 0.05$ (Not Significant)

No-ozone and Ozone $F = 0.10$ (Not Significant)

Interactions: Not Significant

TABLE 8. Stereoscopic Acuity

AGE (yr)	NO-OZONE				OZONE			
	Smokers		Nonsmokers		Smokers		Nonsmokers	
	(Arc Seconds)				(Arc Seconds)			
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
40 to 49	31.3	20.7	28.5	25.2	36.0	33.7	28.0	25.3
50 to 59	23.0	9.5	29.0	17.3	28.0	17.5	29.5	17.1

F-Ratios: Age Groups F = 0.30 (Not Significant)

Smokers and Nonsmokers F = 0.02 (Not Significant)

No-ozone and Ozone F = 1.28 (Not Significant)

Interactions: Not Significant

TABLE 9. Changes in Vertical and Lateral Phorias From No-Ozone to Ozone Conditions

CHANGES WITH OZONE	40 TO 49 YR								50 TO 59 YR							
	Vertical				Lateral				Vertical				Lateral			
	Smokers		Non-Smokers		Smokers		Non-Smokers		Smokers		Non-Smokers		Smokers		Non-Smokers	
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Improved	1	10	2	20	4	40	3	30	2	20	1	10	1	10	4	40
Degraded	1	10	0	0	0	0	1	10	2	20	1	10	2	20	1	10
No Change	8	80	8	80	6	60	6	60	6	60	8	80	7	70	5	50
Totals	10	100	10	100	10	100	10	100	10	100	10	100	10	100	10	100

TABLE 10. Accommodation

AGE (yr)	NO-OZONE						OZONE					
	Smokers			Nonsmokers			Smokers			Nonsmokers		
	(cm)		(D)	(cm)		(D)	(cm)		(D)	(cm)		(D)
	Mean	S.D.		Mean	S.D.		Mean	S.D.		Mean	S.D.	
						OUT-TO-CLEAR						
40 to 49	27.9	8.5	3.58	28.2	7.1	3.55	30.1	6.6	3.32	27.9	7.1	3.58
50 to 59	24.9	6.0	4.02	29.1	8.0	3.44	27.4	6.4	3.65	30.4	6.9	3.29
F-Ratios:	Age Groups			F = 0.06 (Not Significant)								
	Smokers and Nonsmokers			F = 0.35 (Not Significant)								
	No-ozone and Ozone			F = 8.52 ($p \leq .01$)								
Interactions:	Not Significant											
						IN-TO-BLUR						
40 to 49	30.4	7.1	3.29	26.3	6.0	3.80	31.1	7.4	3.22	26.7	6.4	3.74
50 to 59	29.4	5.2	3.40	33.9	4.4	2.95	30.4	5.4	3.29	32.6	4.9	3.07
F-Ratios:	Age Groups			F = 2.65 (Not Significant)								
	Smokers and Nonsmokers			F = 0.07 (Not Significant)								
	No-Ozone and Ozone			F = 0.12 (Not Significant)								
Interactions:	Not Significant											

TABLE 11. Time to Complete the Farnsworth Panel D-15 Color Test

AGE (yr)	NO-OZONE				OZONE			
	Smokers		Nonsmokers		Smokers		Nonsmokers	
	(s)		(s)		(s)		(s)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
40 to 49	50.0	13.2	42.9	15.3	48.9	11.4	39.4	15.1
50 to 59	51.4	12.6	49.7	12.6	59.0	17.3	46.6	11.5

F-Ratios: Age Groups F = 2.69 (Not Significant)

Smokers and Nonsmokers F = 3.90 (Not Significant)

No-ozone and Ozone F = 0.00 (Not Significant)

Interactions: Not Significant

TABLE 12. Completion Time and Errors of Hand-Eye Coordination Test

AGE (Yr)	NO-OZONE					OZONE			
	Smokers		Nonsmokers			Smokers		Nonsmokers	
	(s)		(s)		TIME	(s)		(s)	
	Mean	S.D.	Mean	S.D.		Mean	S.D.	Mean	S.D.
40 to 49	104.3	40.8	84.2	14.2		98.6	34.6	79.7	15.0
50 to 59	123.4	32.1	114.6	38.7		115.3	35.8	121.8	37.0
F-Ratios: Age Groups	F = 7.97 ($p \leq .01$)								
Smokers and Nonsmokers	F = 1.16 (Not Significant)								
No-ozone and Ozone	F = 0.55 (Not Significant)								
Interactions: Not Significant									
	(No.)		(No.)		ERROR	(No.)		(No.)	
	Mean	S.D.	Mean	S.D.		Mean	S.D.	Mean	S.D.
40 to 49	2.7	3.5	2.5	3.1		2.5	3.1	1.8	2.4
50 to 59	1.8	1.7	4.4	4.7		2.1	2.0	3.8	3.5
R-Ratios: Age Groups	F = 0.52 (Not Significant)								
Smokers and Nonsmokers	F = 0.88 (Not Significant)								
No-ozone and Ozone	F = 0.58 (Not Significant)								
Interactions: Not Significant									

TABLE 13. Blink Rate and Range

AGE (Yr)	NO-OZONE				OZONE			
	Smokers (B/min)		Nonsmokers (B/min)		Smokers (B/min)		Nonsmokers (B/min)	
	BLINK RATE							
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
40 to 49	18.3	9.0	16.7	9.1	17.8	10.5	22.4	9.3
50 to 59	18.1	7.6	9.7	5.6	22.1	9.2	16.0	7.9
F-Ratios: Age Groups	F = 0.86 (Not Significant)							
Smokers and Nonsmokers	F = 1.27 (Not Significant)							
No-ozone and Ozone	F = 15.18 ($p \leq .01$)							
Interactions: Between BC, F = 4.46 ($p \leq .05$). All other interactions not significant.								
	RANGE							
40 to 49	8.1	4.2	7.00	3.8	8.3	5.3	8.7	5.3
50 to 59	7.6	2.8	3.9	1.5	9.6	4.1	6.1	4.3
F-Ratios: Age Groups	F = 1.60 (Not Significant)							
Smokers and Nonsmokers	F = 4.16 ($p \leq .05$)							
No-ozone and Ozone	F = 3.22 (Not Significant)							
Interactions: Not Significant								

TABLE 14. Number and Percentage of Test Subjects With Changes in Visual Fields From No-Ozone to Ozone

CHANGES WITH OZONE	40 TO 49 YR								50 TO 59 YR							
	Smokers				Nonsmokers				Smokers				Nonsmokers			
	RE		LE		RE		LE		RE		LE		RE		LE	
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Improved	3	30	2	20	2	20	4	40	1	10	5	50	2	20	1	10
Degraded	3	30	4	40	2	20	2	20	5	50	1	10	4	40	4	40
No Change	4	40	4	40	6	60	4	40	4	40	4	40	4	40	5	50
Totals	10	100	10	100	10	100	10	100	10	100	10	100	10	100	10	100

TABLE 15. Retinal Bleach Recovery Time

AGE (Yr)	NO-OZONE				OZONE			
	Smokers		Nonsmokers		Smokers		Nonsmokers	
	TIME (s)				TIME (s)			
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
40 to 49	64.2	51.5	80.2	60.8	104.7	89.5	103.0	96.4
50 to 59	76.7	44.9	91.0	60.4	76.5	49.4	93.4	64.4

F-Ratios: Age Groups — F = 0.03 (Not Significant)

Smokers and Nonsmokers — F = 0.33 (Not Significant)

No-ozone and Ozone — F = 4.44 ($p \leq .05$)

Interactions: Not Significant

TABLE 16. Scotopic Vision

AGE (Yr)	NO-OZONE				OZONE			
	Smokers		Nonsmokers		Smokers		Nonsmokers	
	Microlamberts				Microlamberts			
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
40 to 49	0.56	0.25	0.36	0.12	0.59	0.31	0.42	0.24
50 to 59	0.42	0.25	0.67	0.40	0.86	0.53	0.59	0.51

F-Ratios: Age Groups F = 2.40 (Not Significant)

Smokers and Nonsmokers F = 1.07 (Not Significant)

No-ozone and Ozone F = 4.45 ($p \leq .05$)

Interactions: F = 5.59 ($p \leq .05$)

F = 7.07 ($p \leq .05$)

Remaining interactions not significant.

TABLE 17. The Light Energy Required to Identify Numerals Under Scotopic Conditions

AGE (Yr)	NO-OZONE								OZONE							
	Smokers				Nonsmokers				Smokers				Nonsmokers			
	20/25	20/35	20/60	20/105	20/25	20/35	20/60	20/105	20/25	20/35	20/60	20/105	20/25	20/35	20/60	20/105
	Millilamberts				Millilamberts				Millilamberts				Millilamberts			
40 to 49																
Mean	6.30	4.21	2.01	0.49	6.17	6.23	2.79	0.41	7.22	5.73	2.43	0.78	5.60	4.10	1.93	0.54
S.D.	2.50	2.58	1.65	0.33	3.41	3.58	1.79	0.20	2.97	3.49	1.30	0.80	3.16	3.21	1.49	0.34
50 to 59																
Mean	6.34	4.26	1.49	0.29	6.52	4.83	3.13	0.34	6.27	4.32	2.06	0.47	6.18	4.77	2.30	0.45
S.D.	3.41	3.32	1.80	0.20	2.23	2.77	3.32	0.19	3.53	3.74	2.38	0.58	3.79	2.83	2.92	0.35

F-Ratios:		20/25	20/35	20/60	20/105
	Age Groups	F = 0.00 (Not Significant)	0.33 (Not Significant)	0.00 (Not Significant)	2.41 (Not Significant)
	Smokers and Nonsmokers	F = 0.22 (Not Significant)	0.15 (Not Significant)	0.80 (Not Significant)	0.42 (Not Significant)
	No-ozone and Ozone	F = 0.00 (Not Significant)	0.11 (Not Significant)	0.28 (Not Significant)	5.28 ($p \leq .05$)

Interactions: At 20/35, BC, F = 4.20 ($p \leq .05$). Remaining interactions were not significant.

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SECTION VI

DISCUSSION AND CONCLUSIONS

C. E. Melton

The presence (+) or absence (-) of adverse effects of ozone on the various measurements made in this study are shown in Table 18. The reported effects on mentation (3) were not confirmed by the measurement of short-term memory in this study, nor were effects seen on heart rate. The effects that were seen were related to contact of ozone with body surfaces such as the respiratory epithelium or the exposed portion of the eye. In all probability the several effects on vision were related to tearing and, perhaps, corneal swelling rather than to blood-borne agents acting on the retina. The visual effects are inconsistent. They are difficult to explain if it is assumed that the effects are caused by toxic substances in the blood. For example, ozone differentiates, with a high level of probability, between "positive" accommodation (in-to-blur) and "negative" accommodation (out-to-clear). In order to explain this finding, one would have to postulate different neuromuscular mechanisms for "positive" and "negative" accommodation, one of which was impaired by ozone and one not impaired. Sympathetically mediated active distance accommodation has been claimed to exist to account for the dioptic change from the rest point of accommodation to infinity, but not for dioptic changes from the near point to the rest point (4). These ocular effects are more reasonably explained by eye irritation complained of subjectively by the subjects and shown objectively by the increased blink rate of some subjects in ozone.

It appears that smoking does mitigate the pulmonary symptoms of ozone exposure. Adverse spirometric effects of ozone are more numerous among nonsmokers than among smokers. This mitigating effect of smoking may be related to ozone scrubbing by residual smoke products in the deep lung, though such an effect could not influence subjective symptoms in the upper portion of the respiratory tract. It is also possible that smoking desensitizes the respiratory passages to sensations caused by acute exposure to ozone.

The data of this study generally confirm those of our earlier studies in that 0.30 ppmv ozone is at or near the threshold for adverse effects of ozone (2). Apparently, there is a good deal of individual variability. Earlier studies showed 0.30 ppmv ozone to be generally ineffective on sedentary nonsmoking subjects in their third decade of life.

The question remains somewhat open regarding the interaction of ozone level and exercise. Folinsbee has carried out some studies in this regard and has found that 0.10 ppmv ozone at ground level was innocuous with heavy exercise (1). We found 0.20 ppmv ozone to be innocuous to flight attendant surrogates undergoing intermittent mild exercise at altitude.

TABLE 18. Summary of Ozone Effects

Heart Rate and Short-Term Memory	(-)
Symptoms	
40-49 S	(-)
50-59 S	(+)
40-59 S	(+)
40-49 NS	(++)
50-59 NS	(-)
40-59 NS	(+)
40-59 S and NS	(++)
Spirometry	
40-49 NS	(+) FVC
50-59 NS	(+) FVC, $FEF_{75-95\%}$
40-59 NS	(+) FVC, FEV_1
40-49 S	(+) FVC
50-59 S	(-)
40-59 S	(-)
40-59 S and NS	(+) FVC, FEV_1, $FEF_{75-95\%}$
Vision	
Photopic Distant Acuity	(-)
Stereoscopic Acuity	(-)
Phoria	(-)
Accommodation	(+)
Color Vision	(-)
Hand-Eye Coordination	(-)
Blink Rate	
Smokers	(-)
Nonsmokers	(+)
Mesopic Vision	
Visual Fields	(-)
Retinal Bleach Recovery	(+)
Scotopic Vision	
Acuity	(+)
Numerical Recognition	(+)
Eye Irritation	(+)

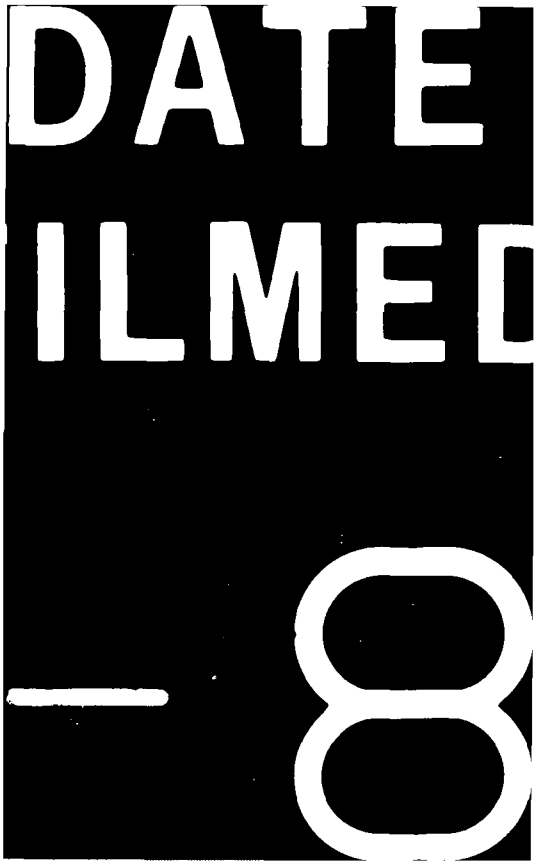
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